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Blushing in rosacea sufferers

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Short title: Blushing in rosacea

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Abstract

Objective. Rosacea is characterized by extremely sensitive skin and persistent facial flushing, perhaps initiated or exacerbated by frequent or intense blushing. To investigate this, blushing was assessed in rosacea sufferers and controls during embarrassing laboratory tasks.

Methods. Changes in forehead blood flow were monitored with laser Doppler fluxmetry in 31 rosacea sufferers (12 with severe symptoms and 19 with mild symptoms) and 86 controls while singing, giving an impromptu speech, and listening to recordings of these activities.

Results. Changes in forehead blood flow were similar in rosacea sufferers and controls, and were similar in subgroups with mild and severe rosacea. Even so, rosacea sufferers thought that they blushed more intensely and were more embarrassed than controls during most of the tasks. Likewise, changes in forehead blood flow were similar in participants with mild and severe rosacea. Nevertheless, ratings of embarrassment and blushing were greater in those with severe than mild symptoms. Within the rosacea group, increases in blood flow while singing were greatest in participants with the highest blushing ratings, whereas increases in blood flow while listening to the speech were greatest in the most embarrassed participants.

Conclusions. These findings do not support the hypothesis that blushing is abnormal in rosacea but, nevertheless, suggest that rosacea sufferers are more aware of and embarrassed by blushing than controls. This might contribute to social anxiety in rosacea sufferers.

Key words: blushing; embarrassment; rosacea; skin blood flow

Introduction

Rosacea is a dermatological disorder involving the cheeks, nose, chin and forehead that typically affects fair-complexioned women and men of north or west European descent aged between 30 and 50 years [1]. In population-based European studies, the prevalence of rosacea was estimated to be between 2 – 10% [2 – 4]. It is characterized by extremely sensitive skin and persistent flushing, and may be accompanied by acne-like facial papules or pustules, prominent facial capillaries, swelling of sebaceous glands, skin thickening and ocular discomfort [1, 5, 6].

Psychological factors such as stress and anxiety, and emotions such as anger and embarrassment, may aggravate flushing in rosacea [7, 8]. Indeed, in early concepts of rosacea, it was thought that “blushing which is produced by the slightest provocation forms one of the early symptoms of the disease, frequent repetition producing enlarged blood vessels and finally tissue hypertrophy” [9, pages 123-124]. Similarly, Klaber and Wittkower [10] proposed that feelings of guilt, inferiority or shame provoked repetitive bursts of blushing, and eventually produced a “permanent blush” [see also 11]. In Klaber and Wittkower’s study, 35 of 50 patients (compared with 11 of 50 controls) described features of social anxiety as children which usually persisted into adulthood. Most patients reported that excitement or worry brought on hot flushes and that emotional stress intensified the severity of rosacea. Moreover, in 33 cases, the onset of rosacea was preceded by acute emotional trauma or prolonged emotional stress. Thus, frequent or intense blushing might increase vulnerability to rosacea.

In a study in our laboratory, the Blushing Propensity Scale [12] was administered to 19 patients with mild rosacea and another 12 with more severe rosacea [13]. Blushing propensity scores were greater in severe than mild rosacea sufferers or controls, indicating that participants with severe symptoms thought that they blushed readily in a range of

social situations. However, as scores on the Blushing Propensity Scale are associated with self-focused attention and heightened social anxiety [12, 14 – 16], elevated scores could represent anxiety about blushing rather than blushing *per se*. To investigate this in the present study, laser Doppler fluxmetry was used to monitor changes in facial blood flow during stressful laboratory tasks (singing, giving a speech and listening to recordings of these activities). It was hypothesized that blushing would be greater in rosacea sufferers than controls, and would be greater in participants with severe than mild rosacea.

Method

Participants

The rosacea sample consisted of 19 participants with mild facial flushing and sporadic papules and pustules, and another 12 with more severe flushing and/or a dense concentration of facial papules and pustules (23 women and eight men aged between 19 and 68 years, mean age \pm S.D. 46.5 ± 12.1 years) [13]. The diagnosis of rosacea was confirmed by a general practitioner or dermatologist. The control group consisted of 67 women and 19 men aged between 17 and 59 years (mean age 29.2 ± 12.4 years) without a history of rosacea. Because we wished to assess blushing in rosacea, individuals who took daily medication for rosacea or for any other medical condition were excluded. Each participant provided informed consent for the procedures, which were approved by the Institutional Ethics Committee.

Procedures

Participants were tested individually in a small room maintained at $21 \pm 2^\circ\text{C}$. To monitor changes in skin blood flow, a laser Doppler flow probe was inserted into a probe holder attached 2-3 cm above the right eyebrow. Doppler-shifted laser beams were detected by an MBF3D Laser Blood Flow Monitor (Moor Instruments Ltd., England) and converted into a digital signal 200 times per second via an MP100 data acquisition system (Biopac Systems, Goleta, California). Laser Doppler fluxmetry is a well-validated method of

measuring relative changes in skin blood flow [17], and has previously been used to detect increases in forehead blood flow associated with blushing [18, 19].

The tasks were presented in fixed order at three minute intervals. During the rest periods between tasks, participants were instructed to sit quietly and to keep movements to a minimum. Before and after each task, participants rated embarrassment and blushing on numerical scales ranging between 0 and 10 where 0 corresponded to “no embarrassment” or “not blushing at all”, 1-4 to grades of “mild”, 5-8 to “moderate”, and 9-10 to “extreme” embarrassment or blushing.

After sitting quietly for ten minutes, participants were asked to sing “Old Macdonald had a farm” for three minutes while the experimenter monitored changes in facial blood flow on a computer screen in an adjacent room. The door between the two rooms was left ajar so that the experimenter (DS) could hear the participant singing. To aid recall, a list of various animal noises was provided for each new verse of the song. Three minutes after the conclusion of the song, the experimenter entered the room and sat opposite the participant while listening to a tape recording of the first two minutes of singing. Three minutes later, participants were asked to give a three-minute impromptu speech on “Should there be a death penalty in this world?”. Three minutes after the conclusion of the speech, the experimenter joined the participant and listened to the first two minutes of the recorded speech.

Data reduction and statistical approach

Mean blood flow during and after each of the tasks was expressed as the percent change from levels recorded during the final minute of baseline. These responses were investigated in a Group (rosacea, control) x Task (singing or speech) x Condition (performing or reviewing the task) x Block (during versus after the task) analysis of variance for repeated measures (SPSS version 17). Ratings of embarrassment and

blushing before and after each task were investigated in similar analyses. Age was included as a covariate in these analyses because participants with rosacea were significantly older than controls ($p < 0.001$). In a second series of analyses, patients and controls were matched for age (within six years) and sex. Two participants with rosacea aged 68 years were excluded from these analyses because age-matched controls were not available. Age was similar in the age- and sex-matched groups [45.0 ± 11.1 years in the rosacea sample versus 43.7 ± 10.1 years in controls, $t(56) = 0.50$, not significant].

Analyses were also run within the rosacea group to compare changes in blood flow and ratings in those with mild versus severe symptoms. Age was not included as a covariate in these analyses because mean age was similar in both groups.

Results are reported as the mean \pm S.E.

Results

Rosacea versus controls

Blushing and embarrassment ratings were associated with each other during each of the four experimental conditions (Table 1). Ratings were unrelated to changes in forehead blood flow in controls whereas, within the rosacea group, increases in blood flow while singing were greatest in participants with the highest blushing ratings [$r(29) = 0.39$, $p < 0.05$]. In addition, increases in blood flow while listening to the speech were greatest in the most embarrassed participants [$r(29) = 0.43$, $p < 0.05$]. However, these correlations failed to achieve statistical significance when Bonferroni's procedure was used to correct for multiple comparisons.

In the group as a whole, ratings of embarrassment and blushing were greater for singing than for the speech [for embarrassment, main effect for Task: $F(1,114) = 6.56$, $p < 0.05$; for blushing, main effect for Task: $F(1,114) = 10.2$, $p < 0.01$] (Figures 1A – 1D). However, ratings differed between groups. In particular, embarrassment and blushing

ratings increased to much the same extent in the rosacea group in all four conditions, whereas ratings peaked in controls when they listened to the recording of themselves singing [for embarrassment, Group x Task x Condition $F(1,114) = 4.92$, $p < 0.05$; Group x Condition x Block $F(1,114) = 10.9$, $p < 0.001$; for blushing, Group x Condition x Block $F(1, 114) = 4.98$, $p < 0.05$] (Figures 1A – 1D). Similar effects were identified in the age- and sex-matched groups [for embarrassment, Group x Condition $F(1,56) = 4.16$, $p < 0.05$; Group x Condition x Block $F(1,56) = 9.68$, $p < 0.01$; for blushing, Group x Condition $F(1,56) = 4.14$, $p < 0.05$; Group x Condition x Block $F(1, 56) = 4.91$, $p < 0.05$].

When expressed in arbitrary units (A.U.), flux was similar in rosacea patients and controls before the tasks began [0.24 ± 0.01 A.U. in patients versus 0.22 ± 0.01 A.U. in controls, $t(115) = 1.22$, not significant]. When expressed as the percent change from baseline, increases in flux were greater when performing than when reviewing tasks [main effect for Condition, $F(1,114) = 16.9$, $p < 0.001$] (Figures 1E and 1F). However, vascular responses did not differ significantly between groups during any of the tasks (none of the effects that included Group achieved statistical significance in analyses that incorporated age as a covariate or in analyses of age- and sex-matched groups).

Severe versus mild rosacea

Participants with severe rosacea reported greater increases in embarrassment during each of the tasks than participants with mild symptoms [Group x Block interaction $F(1,29) = 7.76$, $p < 0.01$] (Figures 2A and 2B). They also reported more blushing [main effect for Group $F(1,29) = 5.46$, $p < 0.05$; Group x Task x Block $F(1,29) = 7.13$, $p < 0.05$] (Figures 2C and 2D).

Flux was greater at baseline in patients with severe than mild rosacea [0.28 ± 0.02 A.U. versus 0.22 ± 0.01 A.U., $t(29) = 3.06$, $p < 0.01$], and this difference persisted throughout the tasks [main effect for Group $F(1,29) = 8.65$, $p < 0.01$; Group x Block

interaction $F(1,29) = 5.00, p < 0.05$]. However, when expressed as the percent change from baseline, vascular responses were similar in both groups (Figures 2E and 2F).

Discussion

The aim of this study was to determine whether blushing was greater in rosacea sufferers than controls during embarrassing laboratory tasks. Contrary to expectations, changes in forehead blood flow were similar in both groups, and were similar in patients with mild and severe rosacea. Even so, rosacea sufferers were more embarrassed and thought that they blushed more intensely during most of the tasks than controls. Likewise, changes in forehead blood flow were similar in patients with mild and severe rosacea; nevertheless, ratings of embarrassment and blushing generally were greater in patients with severe than mild symptoms.

Vascular responses in rosacea

Although flushing is one of the hallmarks of rosacea, the pathogenesis of this sign is unclear. Borrie [20] visually inspected blanching and flushing to intradermal administration of adrenaline, noradrenaline, histamine, acetylcholine and carbachol in rosacea patients and controls, but could detect no differences between groups. Wilkin [21] reported that hot liquids provoked flushing in patients with rosacea, and proposed that the exchange of heat from blood in the internal jugular vein or cavernous sinus to the arterial supply of the hypothalamus triggered flushing. To explore this idea, Brinnel et al. [22] measured tympanic, esophageal, forehead and hand temperatures in four rosacea patients and two controls before, during and after one hour of body heating at 38-39°C, with fanning to cool the face during the last half hour; in addition, blood flow through the emissary veins that connect the facial circulation with the intracranial cavernous sinus was monitored with Doppler ultrasound. Flushing in patients with rosacea was associated with signs of impaired blood flow through the emissary veins, suggesting that a fault in

the countercurrent heat exchange system prevented diversion of cool venous blood from the facial circulation to intracranial structures. However, this fault might not fully account for flushing in rosacea because changes in facial temperature during body heating and cooling appear to be similar in rosacea patients and controls [23].

In the present study, increases in forehead blood flow were comparable in patients and controls during the series of stressful tasks, and were similar in patients with mild and severe rosacea. Thus, the findings do not support the view that increases in facial blood flow during blushing are greater than normal in rosacea. However, further investigation is required to determine whether a deepening of facial redness evoked by blushing in people with rosacea is more noticeable than the pinkness typically associated with blushing in people without rosacea. In line with this possibility, Voncken and Bögels [24] reported that blushing was more conspicuous in patients with a fear of blushing than in controls, despite similar increases in the DC component of a photoplethysmograph signal (an index of blood flow). Importantly, high basal levels of blood flow might have accentuated the visibility of blushing in Voncken and Bögels' study, because cheek temperature was greater in patients than controls throughout the experiment. Kligman [11] distinguished between blushing – generated by an emotional response that usually lasts only a few minutes – and flushing, which typically lasts five minutes or more and may be triggered by a variety of stimuli (e.g., alcoholic beverages, spicy foods, heat, sunlight, exercise, or prolonged psychological stress). As blushing dissipated quickly in rosacea sufferers after singing and giving an impromptu speech, blushing did not appear to evoke or aggravate flushing in the present study. Yamasaki and Gallo [25] proposed recently that the innate immune system triggers an abnormal inflammatory reaction that mediates the symptoms of rosacea [26, 27]. If so, erythema may be due to chronic inflammation.

Psychological responses in rosacea

In on-line surveys conducted by the National Rosacea Society of America (http://www.rosacea.org/rr/2007/spring/article_3.php), many of the respondents reported low self-esteem and embarrassment due to facial redness and disfigurement. These findings have been corroborated in small-scale surveys [28 – 30]. Although early impressions that rosacea is a manifestation of emotional trauma or other psychiatric difficulties [31, 32] do not apply to most patients seen in dermatological practice [33 – 35], rosacea may have a major impact on quality of life [36 – 38]. For example, people with severe rosacea prefer to avoid situations that might involve scrutiny by others [13]. In addition, self-reported depression is greater in patients with rosacea than in patients with other dermatological disorders [34]; indeed, co-morbidity between rosacea and major depressive disorder may have important clinical implications [35].

In the present study, participants with rosacea, particularly those with severe symptoms, reported more embarrassment and thought that they blushed more intensely than controls during most of the stressful tasks. As perceptions of blushing were associated with the degree of embarrassment, these findings suggest that blushing heightened embarrassment. In particular, rosacea sufferers could worry that blushing might draw attention to their persistently flushed face, or that the erythema of rosacea might be misinterpreted as an intense emotional response [13] or a sign of alcoholism [39].

In exploratory analyses, increases in forehead blood flow in rosacea patients were associated with ratings of embarrassment while listening to the speech and with blushing ratings while singing. These associations should be interpreted with caution because statistical significance was lost after correcting for multiple comparisons. Nonetheless, they suggest that increases in facial blood flow during embarrassment might evoke interoceptive cues in rosacea sufferers. In particular, it would be interesting to determine

whether facial stinging or burning intensifies during stressful or embarrassing encounters in patients with rosacea.

Limitations

As the sample of rosacea patients was relatively small, our study might have lacked sufficient power to detect differences between patients and controls, or between subgroups with mild versus severe rosacea. However, it seems unlikely that increases in facial blood flow (expressed as a percentage of baseline) are greater during blushing in rosacea patients than controls because, if anything, differences trended in the opposite direction in the present study.

Rosacea is characterized by erythema. Thus, basal levels of skin blood flow might have differed between patients and controls. Laser Doppler fluxmetry does not measure blood flow in absolute terms because the signal is influenced by variations in dermal microvascular anatomy [40]. Nevertheless, mean flux, measured in arbitrary units, was greater in participants with severe than mild rosacea, suggesting that flux was elevated in this subgroup. Increases in blood flow, although similar in percentage terms, might have different physiological implications when coming off a high versus a low base. This requires further investigation.

The differential diagnosis of rosacea is challenging, as seborrhoeic dermatitis and diseases such as keratosis pilaris and lupus may co-exist with or mimic features of rosacea [1, 11, 39]. Although each patient in our sample had been diagnosed with rosacea by a general practitioner, only some of them had attended a dermatologist. Thus, the possibility of misdiagnosis cannot be ruled out.

Conclusions

Contrary to expectations, rosacea did not influence increases in facial blood flow during psychological stress. Nevertheless, the findings suggest that rosacea sufferers were

more aware of and embarrassed by blushing than controls. Blushing during social interactions might contribute to social anxiety in rosacea sufferers by drawing attention to their persistently flushed face [13]. If so, psychological interventions for a fear of blushing [41, 42] may help to alleviate social anxiety associated with facial flushing in patients with rosacea.

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Table 1

Association between self-report ratings and forehead blood flow during each task

	Embarrassment with Blushing	Embarrassment with Blood Flow	Blushing with Blood Flow
<u>Controls (N = 86)</u>			
Singing	0.65**	-0.01	-0.00
Listening to singing	0.65**	-0.12	-0.09
Speech	0.72**	0.14	0.06
Listening to the speech	0.67**	-0.04	0.02
<u>Rosacea patients (N = 31)</u>			
Singing	0.49**	0.06	0.39*
Listening to singing	0.57**	0.12	0.18
Speech	0.49**	0.17	0.15
Listening to the speech	0.66**	0.43*#	0.16

** Pearson's correlation coefficient statistically significant after Bonferroni's correction.

* Pearson's correlation coefficient statistically significant before but not after Bonferroni's correction.

Correlation significantly greater in rosacea patients than controls (Fisher's r-to-z transformation, $p < 0.05$) [43].

Figure legends

Figure 1. Ratings (\pm S.E.) of embarrassment and blushing, and changes in forehead blood flow (\pm S.E.), in rosacea patients and controls. The values presented in these graphs are residual scores after correcting for age differences between groups.

Figure 2. Ratings (\pm S.E.) of embarrassment and blushing, and changes in forehead blood flow (\pm S.E.), in patients with mild or severe rosacea.



